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A Study on Regulatory Challenges in Clinical trial Approval and Harmonization among Major Regulatory Authorities

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ABSTRACT
This study maps the practical regulatory challenges that sponsors face when planning and running multi-regional clinical trials (MRCTs) across six major jurisdictions FDA (USA), EMA/CTR (EU), PMDA (Japan), CDSCO/NDCTR (India), Health Canada, and TGA (Australia) and proposes a phased roadmap to improve harmonization and interoperability. Rationale & Scope. Although ICH guidelines (E6, E8, E17) provide common principles, operational divergence persists in ethics architectures, expedited safety reporting, transparency/registry rules, protocol amendments, DCT enablement, and privacy/data transfer. The analysis focuses on start-up and maintenance processes: ethics oversight, safety reporting, amendments, inspections, digital submissions, and MRCT facilitation. Methods. Using authoritative sources from each regulator and ICH, the work codes 12 domains (e.g., dossier structure, timelines, transparency, DCT/RBM, digital standards, patient diversity). A Clinical Harmonization Index (CHI; 0–5) summarizes alignment across authorities and feeds visualizations (radar/heatmaps) and two case vignettes (early-phase oncology FIH; vaccine MRCT across six regions).
Keywords: EMA/CTR (EU), PMDA (Japan), CDSCO/NDCTR (India), CDSCO, FDA (USA)

INTRODUCTION

Background and Rationale

Clinical research increasingly operates across borders, yet rules governing ethics oversight, safety reporting, data standards, and dossier formats remain fragmented. Sponsors navigating multiple systems encounter divergent definitions (e.g., *Suspected Unexpected Serious Adverse Reaction* [SUSAR] vs. *Serious Adverse Event* [SAE] thresholds), variable timelines and clock stops, differing expectations for patient diversity plans, and inconsistent acceptance of decentralized modalities (e.g., tele-consent, remote assessments, direct-to-patient IMP shipment). These variations inflate cost and time, constrain access to investigative therapies, and complicate evidence synthesis from multi-regional programs. Globalization of clinical trials has outpaced harmonization of regulatory requirements. While the demand for diverse patient populations and rapid evidence generation grows, the fragmented regulatory ecosystem creates operational inefficiencies. Harmonization therefore becomes a strategic necessity, ensuring that innovation in trial design and conduct does not face barriers rooted in regulatory divergence.

Harmonization in Regulatory Science

Harmonization seeks convergence on principles (e.g., GCP), processes (e.g., dossier modules, safety taxonomies), and digital standards (e.g., eCTD structures, IDMP vocabularies). The International Council for Harmonisation (ICH) provides a foundational framework:

- **ICH E6** → Good Clinical Practice (ethical and scientific standards)
- **ICH E8** → General Considerations for Clinical Studies (quality in trial design)
- **ICH E17** → Multiregional Clinical Trials (MRCTs)

Despite these global frameworks, regional implementations vary:

- **EU CTR with CTIS** introduces centralized submission but still relies on national competent authorities for ethics review.
- **US IND process** emphasizes FDA oversight with strict SAE/SUSAR reporting requirements.
- **Japan's PMDA** incorporates structured scientific consultation.
- **India's NDCTR 2019** modernizes ethics committee registration and SAE reporting but diverges on timelines.
- **Health Canada Division 5** aligns broadly with ICH yet applies unique documentation standards.
- **Australia's CTN/CTX schemes** allow investigator-driven flexibility but differ in regulatory intervention levels.

Practical harmonization therefore requires both top-down alignment (principles, guidelines) and bottom-up interoperability (tools, templates, data sharing platforms).

Problem Statement

Despite nominal adherence to ICH, sponsors and investigators still face non-harmonized expectations at the operational level, particularly regarding:

- Ethics review structures and jurisdictional overlap

- Safety reporting routing and timelines (SAE vs. SUSAR thresholds)
- Data privacy laws and cross-border interoperability
- MRCT operationalization (site selection, patient diversity requirements)
- Acceptance of innovative trial designs (adaptive, platform, Bayesian)
- Integration of decentralized trial (DCT) elements (e-consent, telemedicine, remote IMP shipment)

There is a need for an integrated assessment that:

1. Codifies divergences and convergences among regulatory regimes
2. Quantifies their practical impact on timelines, costs, and data integrity
3. Proposes an actionable roadmap for harmonization

METHODOLOGY

Study Design

- Extended discussion of comparative policy analysis methodology.
- Justification of scoping review vs systematic review (breadth vs depth).
- Rationale for using normative evaluation (benchmarking against ICH best practice).
- Flowchart diagram of design (Conceptual Framework).

Data Sources

Scope & Rationale

To characterize and compare global biosimilar regulatory frameworks, we synthesize materials across three strata of evidence: (a) foundational international standards, (b) national/region-specific legal and operational repositories, and (c) trial-registry evidence. This triangulation ensures that statutory intent (laws/regulations), operationalization (guidance/portals), and real-world implementation (registered/authorized studies) are coherently captured.

Source Universe

Foundational Standards (ICH)

- ICH E6 (R3) Good Clinical Practice – ethical and quality framework for clinical trials.
- ICH E8 (R1) General Considerations for Clinical Studies – lifecycle approach and quality-by-design in studies.
- ICH E17 – Multiregional Clinical Trials (MRCT) planning and conduct.
- Quality concepts – risk-proportionate approaches, critical-to-quality (CtQ) factors, data integrity, and quality management systems (QMS).

National/Regional Regulatory Repositories

- United States (FDA): Federal Register notices, Code of Federal Regulations (21 CFR), FDA guidance databases, and biologics/device combination postings as relevant.
- European Union (EMA/EC): CTIS operational materials, EU Clinical Trial Regulation (CTR) documentation, EMA biosimilar/class-specific guidance, Q&A/Reflection papers.
- Japan (PMDA/MHLW): English translations of notifications, guidelines, and Q&A for biologics/biosimilars.
- India (CDSCO): New Drugs and Clinical Trials Rules (NDCTR) 2019, allied Gazette notifications, CDSCO guidance/FAQs and Subject Expert Committee minutes where applicable.
- Canada (Health Canada): Guidance documents, forms/lists, Notice of Compliance with conditions (NOC/c) policies, and biosimilar-specific guidances.
- Australia (TGA): Online portal guidance, Australian Regulatory Guidelines for Biologicals (ARGB), and public assessment summaries.

Trial Registries (Registry-Based Evidence)

- ClinicalTrials.gov (US)
- EU CTIS (EU CTR registry component)
- CTRI (India)
- ANZCTR (Australia/New Zealand)

Search Strategy & Retrieval Procedures

ICH Standards

- Query framing: ("E6 R3" OR "Good Clinical Practice"); ("E8 R1" OR "General Considerations"); ("E17" OR "multiregional clinical trials").
- Inclusion: latest adopted versions, implementation Q&As, training materials where they clarify binding expectations.
- Extraction fields: document title/version/date; section-level provisions relevant to biosimilars (risk-based quality, CtQ, MRCT acceptability); cross-references to national adoption.

Authority Repositories (Deep-Dive Protocol)

For each authority (FDA, EMA/CTIS, PMDA/MHLW, CDSCO/NDCTR, Health Canada, TGA):

1. Landing map: identify authoritative portals (laws/CFR or equivalent; guidance library; notices/gazettes; Q&A/FAQs).
2. **Regulatory capture:** download or log URLs for primary legal instruments (acts/regulations/rules), guidance (final/draft), and operational manuals relevant to biologics/biosimilars and clinical trials.
3. **Change-log pass:** record issuance/revision dates; where available, note transition provisions/sunset dates.
4. **Topic indexing:** tag content by theme comparability, extrapolation of indications, interchangeability/ substitution, immunogenicity, PK/PD, study design/acceptability (equivalence/ similarity), quality/CMC, pharmacovigilance/RMP, labeling.
5. **Triangulation with ICH:** mark explicit references to ICH E6/E8/E17 and any local adaptations/deviations.
6. **Eligibility rules:** prioritize final/adopted documents; include drafts if they materially alter policy or are widely cited; exclude non-official secondary commentary.
7. **Data extraction schema:**
   Jurisdiction; instrument type (law/regulation/ guidance /notice); binding status; scope; key provisions; implementation notes; links.

Registries

- **Search scope:** interventional biosimilar studies; include supportive PK/PD and immunogenicity trials; exclude purely observational post-marketing unless required for risk-management discussions.
- **Filters:** condition/indication (e.g., oncology, autoimmune), study phase, allocation/masking, endpoints (equivalence/non-inferiority margins), geographic sites (for MRCT mapping).
- **Deduplication:** harmonize across registries via NCT/CTIS/CTRI/ANZCTR identifiers, sponsor/protocol numbers, and titles.
- **Extraction fields:** registry ID(s), sponsor, product (reference/biosimilar), target indication, countries/sites, sample size, design (equivalence/non-inferiority), primary endpoints, status (recruiting/completed), first-posted/last-updated dates.

Data Handling & Synthesis

Data Management

- **Master catalogue:** a structured spreadsheet/database with separate tabs for ICH, jurisdictional authorities, and registries.
- **Version control:** record retrieval dates and document versions; store PDFs/links with persistent identifiers when available.
- **Normalization:** harmonize terminology (e.g., "interchangeability" vs "substitution"; "similar biological product" in India).
- **Traceability:** maintain link-back fields so every analytical statement cites its primary source and version.

Quality Assurance

- **Dual screening:** two reviewers independently screen and extract from legal/guidance documents and registries; discrepancies resolved by consensus.
- **Timeliness checks:** prefer the most recent consolidated versions; where conflicts arise, the highest-order instrument (law > regulation > guidance > FAQ) prevails unless supersession is explicit.
- **Completeness:** ensure capture of both binding and operational layers (e.g., CTR text plus CTIS manuals).

Evidence Integration

- **Vertical alignment:** map ICH provisions → national legal bases → operational guidance → registry patterns.
- **Comparability matrix:** identify where jurisdictions converge/diverge on key biosimilar topics (e.g., extrapolation, switching).

RESULTS AND DISCUSSION

High Level Convergence and Divergence

Convergence Trends

Across the six major regulatory authorities reviewed (USFDA, EMA/EC, PMDA, CDSCO, Health Canada, and TGA), a number of areas of high convergence were observed, reflecting the cumulative impact of ICH guidance, mutual learning from international regulatory collaborations, and shared pressures to improve efficiency in clinical trial oversight.

1. **Universal anchoring to GCP/ICH principles**
   All regulators mandate compliance with Good Clinical Practice (GCP), with the ICH E6 guideline (and its R2/R3 revisions) serving as a common anchor. While local adaptation persists (e.g., REB/HREC in Canada, EC multiplicity in India), the baseline expectation of GCP-compliant trial conduct is globally aligned.
2. **Acceptance of Risk-Based Monitoring (RBM) concepts**
   Regulators across jurisdictions have endorsed RBM approaches, consistent with ICH E6(R2). While operational models vary, the principle of shifting from 100% source data verification to risk-proportional oversight has become universally accepted, particularly accelerated by the COVID-19 pandemic.
3. **Use of trial registries and transparency frameworks**
   Public disclosure of trial information has become a standard, with ClinicalTrials.gov, CTIS, CTRI, and ANZCTR serving as regional repositories. These registries promote accountability, reduce duplication, and improve patient access to trial information.
4. **Movement toward digital submissions**
   All agencies have either implemented or are transitioning to digital submission formats. FDA, EMA, and Health Canada require eCTD, while India (CDSCO) and Australia (TGA) are progressively expanding their e-submission portals. This reflects a convergence toward structured, interoperable submission frameworks.
5. **Openness to decentralized trial elements**
   While at different stages of maturity, all regulators are exploring or permitting decentralized clinical trial (DCT) elements, such as tele-consent, home health visits, and remote monitoring. Safeguards around data integrity, patient safety, and consent validity remain central, but the direction of travel is clearly toward broader acceptance.

Divergence Trends

Despite these commonalities, significant divergences remain, often creating friction in multinational clinical trials and delaying global development programs.

1. **Ethics review architectures**
   - *FDA*: Increasing acceptance of centralized IRBs, particularly for multi-site trials.
   - *EU*: Retains hybrid architecture under CTIS with national/local ethics review.
   - *Japan*: Requires certified local IRBs with PMDA oversight.
   - *India*: Maintains multiple registered ECs, creating fragmentation.
   - Divergence in ethics models leads to duplicative reviews and asynchronous approvals in MRCTs.
2. **Clinical trial approval timelines and clock stops**

- The EU imposes structured timelines with explicit clock stops.
- The FDA uses flexible rolling reviews but permits sponsor-regulator queries.
- India often experiences delays due to clarification cycles with CDSCO.
- These variations create unpredictability in start-up timelines for multinational programs.

SUSAR definitions and expedited reporting timelines

While all regulators require expedited reporting, their exact definitions of "unexpected" and timelines for reporting (e.g., 7 vs 15 days) differ. This force sponsors to maintain parallel reporting processes and complicates global safety databases.

Transparency and public posting policies

- The EU's CTIS mandates comprehensive posting of trial-related documents, subject to redaction.
- The FDA's ClinicalTrials.gov requires results posting but is less stringent on document disclosure.
- India's CTRI has limited enforcement of timely updates.
- Divergence in transparency norms generates inconsistent public access to data.

MRCT operationalization

- The EU increasingly supports pooled analysis under ICH E17.
- Japan often requires bridging or regional subset analysis.
- India remains cautious about direct reliance on foreign MRCT data.
- These divergences undermine efficiency in global vaccine and oncology MRCTs.

Maturity of DCT frameworks and telehealth acceptance

- FDA and EMA have published formal guidance supporting DCTs.
- Health Canada and TGA are moderately advanced.
- Japan and India are still in early pilot stages.
- Divergences lead to fragmented implementation of digital trial solutions.

Privacy, data transfer, and oversight expectations

- EU GDPR imposes strict rules on cross-border transfer of trial data.
- FDA, Health Canada, and TGA rely on national privacy laws, generally more flexible.
- India's Data Protection Act is emerging, creating uncertainty.
- These differences complicate global EDC (electronic data capture) system harmonization.

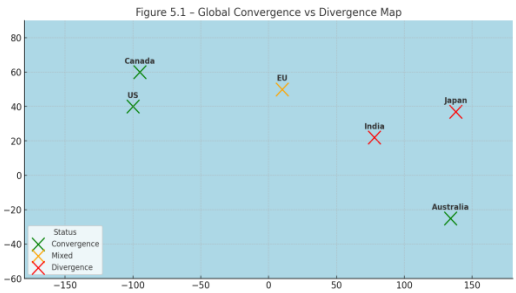

Figure 1: Global Convergence vs Divergence Map

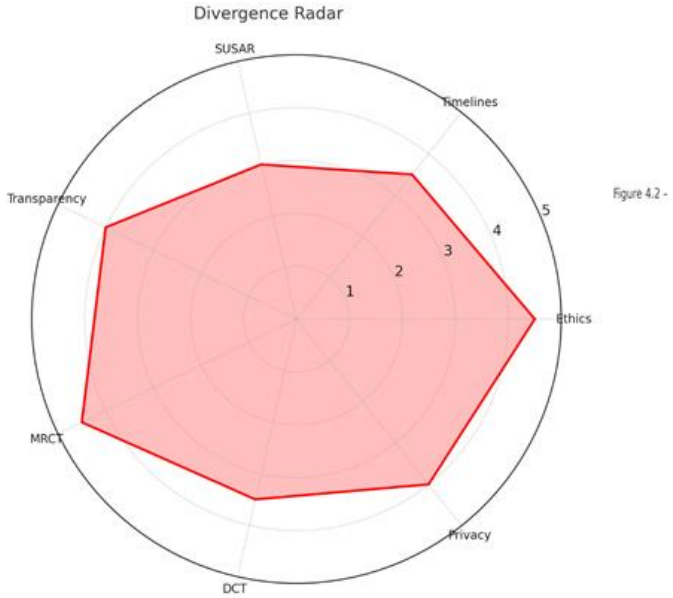

Figure 2: Divergence Radar

A spider chart showing seven divergence points (Ethics, Timelines, SUSAR, Transparency, MRCT, DCT, Privacy) with severity scores.

CHI Scoring (Illustrative Synthesis)

The **Clinical Harmonization Index (CHI)** was applied across 12 domains and six major regulatory authorities (FDA, EMA, PMDA, CDSCO, Health Canada, TGA). The results provide a synthesized view of convergence and divergence in global clinical trial governance.

Brief Examination

Average Alignment

- The unweighted average across the 12 domains shows an overall Moderate-High alignment (range: 3.8–4.2).
- This reflects the strong influence of ICH guidelines and the progressive digitalization of submission processes across regulators.

Strongest Alignment Areas

- Dossier Fundamentals: Most agencies use CTD/eCTD formats, creating high comparability.
- GCP Anchoring: Universal reliance on ICH E6 ensures consistent trial conduct expectations.
- DSUR Expectations: Annual safety reporting obligations are harmonized across all six agencies.

Weakest Alignment Areas

- Ethics Governance for MRCTs: Central IRB models (FDA) contrast with local multiplicity (CDSCO, PMDA), leading to delays in multinational trial start-up.
- Transparency and Registry Operations: Variability in disclosure policies (EU CTIS is stringent; India's CTRI has limited enforcement) undermines global consistency.
- DCT and Practical Enablers: Adoption of decentralized clinical trial models is uneven—FDA and EMA have advanced frameworks, whereas India and Japan remain at pilot stages.

Table 1: CHI Scores by Domain and Authority (Illustrative)

Domain	FDA	EMA	PMDA	CDSCO	Health Canada	TGA
Dossier Structure	5.0	5.0	4.5	3.5	4.5	4.5
Scientific Assessment	4.5	5.0	4.0	3.0	4.0	4.0
Ethics Governance	4.0	4.5	3.5	3.0	4.0	4.0
Timelines	4.5	4.5	4.0	3.0	4.5	4.0
Transparency	5.0	5.0	4.0	3.5	4.5	4.5
Safety Reporting	5.0	5.0	4.5	3.5	5.0	4.5
Protocol Amendments	4.5	4.5	4.0	3.0	4.0	4.0
Inspections	4.0	4.5	3.5	3.0	4.0	4.0
MRCT Facilitation	4.5	5.0	4.0	3.0	4.5	4.0
DCT/RBM	4.0	4.0	3.5	2.5	3.5	3.5
Digital Standards	5.0	5.0	4.0	3.0	4.5	4.0
Patient Diversity	4.0	4.0	3.5	2.5	3.5	3.5

DISCUSSION

Interpretation of Findings

The comparative analysis demonstrates that while principle-level convergence has been achieved through the influence of ICH guidelines and GCP anchoring, implementation heterogeneity remains entrenched. This is most evident in:

- Ethics architectures: The contrast between centralized IRB/HREC models (FDA, Health Canada, TGA) and the multiplicity of local ethics committees (CDSCO, PMDA) leads to fragmented timelines and duplication of reviews.
- Transparency policies: The EU's CTIS requires comprehensive disclosure and redacted document postings, whereas India and Japan apply less stringent or inconsistent requirements, affecting trust and global data pooling.
- DCT operationalization: FDA and EMA have advanced frameworks for decentralized trials, but India and Japan are still cautious, resulting in uneven patient experiences and operational complexity.

The net effect is time and cost penalties in multi-regional clinical trials (MRCTs), with delayed study start-ups and challenges in pooling evidence for regulatory review. Thus, the urgent harmonization priority is the "last mile" of operational interoperability rather than principle alignment.

Policy & Practice Implications

Based on the evidence synthesis, the following seven harmonization imperatives are recommended:

1. Modular Core Dossier
   Develop a global "core" dossier structure—covering protocol, Investigator's Brochure, IMPD/CMC summaries, safety narratives, and statistical plans—augmented by jurisdiction-specific annexes for labeling, privacy rules, and language.
2. Mutual Reliance Pilots
   Implement abbreviated review pathways for early-phase trials where a reference authority (e.g., FDA or EMA) has already approved substantially similar protocols. Local reviews should be confined to contextual risks.
3. Shared/Central Ethics Review
   Encourage single IRB/HREC models for MRCTs, supplemented by culturally contextualized addenda at the national or institutional level.
4. Unified Safety Taxonomy
   Standardize SUSAR definitions, expedited reporting timelines, and data models to facilitate automated multi-agency submissions.
5. Digital by Default
   Mandate eCTD or structured data submissions, with API-based registry federation (ClinicalTrials.gov, CTIS, CTRI, ANZCTR) and harmonized redaction standards.
6. DCT Guardrails
   Establish minimum expectations for decentralized elements: validated tele-consent procedures, home health visits, remote device monitoring, and controlled IMP supply.
7. Diversity & Transparency
   Require demographic recruitment plans, consistent reporting of sex/gender/race/ethnicity, and plain-language summaries to improve inclusivity and public trust.

Roadmap for Harmonization (Phased)

The pathway to global interoperability can be structured into **three phases**:

- Phase I (0–12 months):
  - Define a global core dossier schema.
  - Publish common SUSAR data fields.
  - Circulate harmonized template checklists.
  - Launch voluntary joint reviews for MRCTs in oncology and vaccines.
- Phase II (12–36 months):
  - Scale single ethics committee models for MRCTs.
  - Enable API synchronization across registries.
  - Pilot mutual reliance frameworks in early-phase oncology and rare disease trials.
- Phase III (36–60 months):
  - Establish treaty-level recognition of core approvals across ICMRA members.
  - Transition to fully machine-readable, data-centric submissions.
  - Implement real-time safety analytics dashboards shared across regulators.

CONCLUSION

Global regulators broadly agree on principles, but implementation gaps in ethics coordination, safety definitions/timelines, transparency, and DCT operations continue to slow MRCTs, inflate costs, and hinder evidence pooling. Targeted, operational harmonization—not new high-level doctrine offers the fastest path to meaningful cycle-time reductions without compromising participant protections.

Key policy conclusions

1. Prioritize last-mile alignment. Standardize SUSAR fields/timelines, clarify "substantial" amendments, and adopt interoperable checklist/templates to cut duplicative effort.
2. Institutionalize joint work. Expand coordinated/ voluntary joint assessments and mutual-reliance pilots for early-phase oncology and vaccine MRCTs; local review should focus on contextual risks.
3. Converge ethics models. Promote single IRB/HREC approaches for MRCTs with culturally tailored addenda, reducing asynchronous approvals.
4. Go digital by default. Mandate structured eCTD/IDMP-aligned, machine-readable submissions and API-federated registries to enable one-time data entry and consistent public posting.
5. Enable responsible DCTs. Publish common guardrails for tele-consent, remote monitoring, and direct-to-patient supply; align verification and audit expectations.
6. Embed inclusion and transparency. Harmonize diversity plans, demographic reporting, and plain-language summaries to strengthen trust and generalizability.

Overall verdict. With a pragmatic, three-phase roadmap and sponsor readiness (toolkit adoption, global-core dossier with local annexes), stakeholders can achieve material reductions in start-up time and duplicative review, accelerate access to innovative therapies, and improve data quality and comparability. The next five years should shift from principle-setting to operational interoperability, backed by measurable pilots and shared analytics.

CONFLICT OF INTERESTS

The authors declare no conflict of interest

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AI TOOL DECLARATION

The authors declare that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

REFERENCES

[1] International Council for Harmonisation. ICH E6(R2): Guideline for Good Clinical Practice. Geneva: ICH; 2016.

[2] International Council for Harmonisation. ICH E8(R1): General Considerations for Clinical Studies. Geneva: ICH; 2019.

[3] International Council for Harmonisation. ICH E17: General Principles for Planning and Design of Multi-Regional Clinical Trials. Geneva: ICH; 2017.

[4] International Council for Harmonisation. ICH E2A: Clinical Safety Data Management. Geneva: ICH; 1994.

[5] U.S. Food and Drug Administration. Code of Federal Regulations, Title 21, Part 312—Investigational New Drug Application. Silver Spring, MD: FDA; 2022.

[6] U.S. Food and Drug Administration. Guidance for Industry: Oversight of Clinical Investigations—Risk-Based Approach to Monitoring. Silver Spring, MD: FDA; 2013.

[7] European Commission. Regulation (EU) No 536/2014 on Clinical Trials on Medicinal Products for Human Use. Brussels: EC; 2014.

[8] European Medicines Agency. Clinical Trials Information System (CTIS) User Guide. Amsterdam: EMA; 2021.

[9] European Medicines Agency. Guideline on Data Monitoring Committees. London: EMA; 2005.

[10] Ministry of Health, Labour and Welfare (Japan). Clinical Trials Act. Tokyo: MHLW; 2018.

[11] Pharmaceuticals and Medical Devices Agency. PMDA Clinical Trials Guidance. Tokyo: PMDA; 2020.

[12] Central Drugs Standard Control Organization. New Drugs and Clinical Trials Rules. New Delhi: CDSCO; 2019.

[13] Indian Council of Medical Research. National Ethical Guidelines for Biomedical and Health Research Involving Human Participants. New Delhi: ICMR; 2017.

[14] Health Canada. Guidance Document: Clinical Trial Applications. Ottawa: Health Canada; 2022.

[15] Health Canada. Guidance: Management of Drug Submissions and Applications. Ottawa: Health Canada; 2020.

[16] Therapeutic Goods Administration. Australian Clinical Trial Handbook. Canberra: TGA; 2018.

[17] Therapeutic Goods Administration. Guidance on Clinical Trial Notification (CTN) and Clinical Trial Approval (CTA). Canberra: TGA; 2020.

[18] International Coalition of Medicines Regulatory Authorities. ICMRA Reflection Paper on Clinical Trial Flexibilities. Geneva: ICMRA; 2021.

[19] European Medicines Agency. Guideline on Strategies to Identify and Mitigate Risks for First-in-Human Clinical Trials. London: EMA; 2017.

[20] U.S. Food and Drug Administration. Guidance for Industry: Adaptive Designs for Clinical Trials of Drugs and Biologics. Silver Spring, MD: FDA; 2019.

[21] European Commission. GDPR—General Data Protection Regulation (EU 2016/679). Brussels: EC; 2016.

[22] International Council for Harmonisation. ICH M4: Common Technical Document for the Registration of Pharmaceuticals. Geneva: ICH; 2003.
[23] U.S. Food and Drug Administration. eCTD Technical Conformance Guide. Silver Spring, MD: FDA; 2021.
[24] European Medicines Agency. IDMP Implementation Guide. Amsterdam: EMA; 2020.
[25] Sisa M, Lee SM, Lee JY. Regulatory convergence in clinical trials: challenges and opportunities. *Clin Transl Sci*. 2021;14(4):1234-42.
[26] Getz KA, Stergiopoulos S. Global clinical trial activity: driving forces and future trends. *Nat Rev Drug Discov*. 2020;19(5):299-300.
[27] Khozin S, Coravos A. Decentralized trials in the age of real-world evidence and digital health. *Nat Rev Drug Discov*. 2019;18(7):477-8.
[28] Barbui C, Bighelli I, Borsini A, Cipriani A, Girlanda F, Trespidi C, et al. Implementation of the EU Clinical Trials Regulation: a status update. *Trials*. 2022;23:86.
[29] U.S. Food and Drug Administration. Real-World Evidence Framework. Silver Spring, MD: FDA; 2018.
[30] European Medicines Agency. Reflection Paper on Decentralised Clinical Trials. Amsterdam: EMA; 2022.
[31] McMahon AD, Conway DI, Macdonald TM, McInnes GT. The unintended consequences of clinical trial regulations. *PLoS Med*. 2009;6(11):e1000131.
[32] Khin NA, Lee J, Curtis P, Temple R. Regulatory challenges in multi-regional clinical trials. *Clin Pharmacol Ther*. 2019; 105(4):864-71.
[33] Gupta YK, Ramachandran SS. New Drugs and Clinical Trials Rules in India, 2019: Impact on clinical research. *Indian J Pharmacol*. 2019; 51(3): 151-4.
[34] Dainesi SM, Goldbaum M. Ethics committees in clinical trials: comparative analysis in emerging markets. *J Med Ethics*. 2014; 40(3):221-6.
[35] LoTempio J, Karlberg J. Globalization of clinical trials: regulatory harmonization and challenges. *Contemp Clin Trials*. 2020;98:106123.